APPENDIX 2

Clinical Trials Monitoring Branch

Optional Checklists

Table A
IRB

Investigational Review Board	Comments
IRB: No deficiencies	
IRB (Major Deficiencies)	
Protocol never approved by IRB	
Initial IRB approval documentation missing	
Initial approval by expedited review	
Expedited reapproval for situations other than approved exceptions	
Registration and/or treatment of patient prior to IRB approval	
Reapproval delayed >30 days but < 1 year	
Registration of patient on protocol during a period of delayed reapproval	
Missing reapproval	
Expired reapproval	
Reportable adverse events not reported to IRB	
Lack of documentation of full IRB approval of a protocol amendment that affect more than minimal risk	
IRB (Major Deficiencies)	
Reapproval delayed < 30 days	
Delayed reapprovals for protocols closed to accrual for which all patients have completed therapy	

Table B
Informed Consent Content

Elements Required by Federal Regulations	Deficiencies/Comments
Involves research: purposes; duration of participation; description of procedures; identification of procedures which are experimental	
Description of risks or discomforts	
Description of any benefits to subject or others	
Disclosure of alternative procedures or treatments	
Description of the extent of confidentiality of records	
Explanation regarding compensation and/or whether treatments are available if injury occurs	
Contact for research questions, information regarding subjects rights, and contact for research-related injury	
Participation is voluntary; refusal to participate involves no penalty; subject may discontinue participation at any time	
Other, specify: _____	
Additional elements required by Federal Regulations (when appropriate)	
Unforeseeable risks to subject, embryo or fetus	
Circumstances in which subject's participation may be terminated by investigator without subject's consent	
Additional costs to subject which may result from participation in research	
Consequences of subject withdrawal and procedures for orderly termination of participation by subject	
Statement that new findings which may relate to subject's willingness to continue participation will be provided to subject	
Approximate number of participants	
Statement that a copy of the consent will be given to participant	
Other, specify: _____	

Table C
Review of Accountability of Investigational Agents and Pharmacy Operations

NCI DARFS COMPLETELY AND CORRECTLY FILLED OUT	
COMPLIANCE	**NONCOMPLIANCE**
• Maintain accurate records of the disposition of all CTEP supplied agents using NCI DARFs. • Agents supplied by the Pharmaceutical Management Branch (PMB) for NCI-sponsored protocols should be shipped from PMB directly to the investigator's primary institution or office. • In situations where two or more institutions are operating as a "centralized research base", a centralized pharmacy service can provide pharmacy services (such as agent storage, preparation and accountability) for investigators in the local community, if the investigators designate that pharmacy service as their shipping designee on their FDA form 1572 submitted to PMB. The centralized pharmacy is then permitted to **deliver (not re-ship)** CTEP supplied investigational agents to the investigators' offices, clinics, or other institutions. • Agents may be dispensed, delivered, and accounted for at the treatment site in response to an individual patient's treatment order or a prescription for a single dose or treatment cycle. In this situation, there is no need for satellite accountability records. • If the physician's office, clinic, or other institution receives a multiple day supply of CTEP supplied investigational agents, satellite accountability records must be maintained for each satellite location and copies must be available for review by site auditors.	• Inability to track the receipt, use and disposition of DCTD supplied investigational agents. • NCI DARF not maintained. • Inability to track the agent because of omissions. • Electronic DARFs do not contain all information required on NCI DARF. Paper printout is not identical to the NCI DARF. • Incorrect agent, dose, route of administration, or dates documented on DARF. • Registered patients who have received IND agents are not recorded on DARF. • Systematic incorrect entries on the DARF. • NCI DARF not kept on timely basis. • There are erasures or "whiteouts". • Corrections are not lined out and initialed. • Agent has been transferred to an investigator who is not registered with PMB, DCTD, NCI. • No Satellite NCI DARF. • CTEP supplied investigational agents are repackaged and/or reshipped to other investigators or locations by mail or express carrier.

PROTOCOL AND DRUG SPECIFIC	
COMPLIANCE	**NONCOMPLIANCE**
• Agents received from PMB, DCTD are used only for patients entered onto an approved DCTD-sponsored protocol. • Each agent accounted for separately by protocol. • An agent used for more than one protocol has a separate DARF for each protocol. • Multi-agent protocols have a separate DARF for each agent. • Separate accountability forms maintained for each different strength or dosage form of a particular agent. • [redacted] [redacted]	• Patients identified on DARF are not registered patients. • Substitution with any non-DCTD supplied agents, including commercial agents. • Agents supplied for clinical trials used for pre-clinical or laboratory studies without written approval of PMB. • Lack of source documentation to verify agent supplies distributed to investigators or administered to patients. • Each agent not accounted for separately by protocol. • One DARF used for more than one protocol. • One DARF for a multi-agent protocol. • One DARF used for multiple strengths or dosage forms of an agent. • [redacted] • [redacted] [redacted]

Table C
Review of Accountability of Investigational Agents and Pharmacy Operations

SATELLITE RECORDS	
COMPLIANCE	**NONCOMPLIANCE**
• DARF used at each location where agents are stored and/or dispensed, e.g., main pharmacy, satellite pharmacy, physician's office, or other dispensing areas.	• Satellite and control records are not accurately maintained. • Satellite and control records do not agree.

NCI DARFs KEPT AS PRIMARY TRANSACTION RECORD	
COMPLIANCE	**NONCOMPLIANCE**
• Agent order receipts (Shipment Record of Clinical Drug Request, NIH 986-1) retained and available for review. • Documentation on DARF of other agent transaction: agent returns, broken vials, etc. • Inter-institutional transfer of DCTD investigational agents is approved or authorized by PMB. • Balance on DARF matches supply.	• Agent order receipts (Shipment Record of Clinical Drug Request, NIH 986-1) not retained or not available for review. • Lack of documentation of other agent transactions. • Agents have been borrowed. • Transfer Investigational Drug Form (NIH-2564) not used when transferring agent. • Quantities not accounted for; shelf counts and inventories do not match. • No faxed documentation from PMB of approval for transfer of agent. • No satellite NCI DARF.

RETURN OF DRUG TO NCI	
COMPLIANCE	**NONCOMPLIANCE**
• Return to DCTD agents (a) that are outdated; and (b) that are damaged or unfit for use. • For studies that are completed or discontinued, return DCTD agents to the NCI or appropriately transfer to another NCI protocol.	• DCTD agent not returned to NCI or transferred to an appropriate NCI protocol. • Not using the transfer form when transferring a DCTD supplied agent to an approved NCI protocol.

STORAGE	
COMPLIANCE	**NONCOMPLIANCE**
• Each investigational agent stored separately by protocol. • An agent used for more than one protocol kept in separate physical storage for each protocol. • Agent stored under proper conditions (refrigerator, freezer, etc.) with validation documentation.	• IND not stored separately by protocol. • Agents used for more than one protocol combined in storage. • Agent not stored under proper conditions.

SECURITY	
COMPLIANCE	**NONCOMPLIANCE**
• [redacted] • [redacted]	• Agent stored in insecure dispensing area. • [redacted]

Table D
Patient Case Review

Informed Consent (Major Deficiencies)	Comments D1
Consent form missing	
Consent form not signed and dated by patient	
Consent form signed after patient started on treatment	
Consent form does not contain all required signatures	
Consent form used was not current IRB-approved version at time of patient registration	
Consent form not protocol specific	
Consent form does not include updates or information required by IRB	
Other (Specify, _____)	

Eligibility (Major Deficiencies)	Comments D2
Review of documentation **confirms** patient did not meet all eligibility criteria as specified by the protocol	
Documentation missing; unable to confirm eligibility	
Other (Specify, _____)	

Treatment (Major Deficiencies)	Comments D3
Incorrect agent/treatment used	
Additional agent/treatment used which is not permitted by protocol	
Dose deviations incorrect (error greater than +/- 10%)	
Dose modifications unjustified	
Treatment doses incorrectly administered, calculated or documented	
Unjustified delays in treatment	
Other (Specify, _____)	

Table D
Patient Case Review

Disease Outcome/Response (Major Deficiencies)	Comments D4
Inaccurate documentation of initial sites of involvement	
Tumor measurements/evaluation of status or disease not performed according to protocol	
Protocol-directed response criteria not followed	
Claimed response (PR, CR, etc) cannot be verified	
Failure to detect cancer (as in a prevention study) or failure to identify cancer progression	
Other (Specify, _____)	

Toxicity (Major Deficiencies)	Comments D5
Grades, types, or dates/duration of serious toxcities inaccurately recorded	
Toxicities cannot be substained	
Follow-up studies necessary to acess toxicities not performed	
Failure to report a toxicity that would require filing an Adverse Event Reaction(AER)	
Recurrent under- or over-reporting of toxicities	
Other (Specify, _____)	

General Data Quality (Major Deficiencies)	Comments D6
Recurrent missing documentation e.g., charts	
Protocol-specified laboratory tests not documented	
Protocol-specified diagnostic studies not documented	
Frequent data inaccuracies	
Errors in submitted data	
Delinquent data submission	
Other (Specify, _____)	